REMARKS

The specification is objected to for use of lower case for trademarks.

Applicants are amending this application to correct any inadvertent errors in use of the trademarks in the specification.

The specification is objected to because the sequences on page 21 do not have sequence identification numbers.

Applicants are amending the application to enter the sequence listing into the specification.

Applicants are enclosing herewith

(1) a Computer Readable Form ("CRF") of the sequence listing, and (2) a paper copy of the sequence listing.

The undersigned attorney of record for the applicant hereby declares (1) that the content of the CRF of the sequence listing, and the paper copy are the same and includes no new matter that goes beyond the disclosure set forth in the specification as originally filed and (2) that the undersigned is registered to practice before the U.S. Patent and Trademark Office.

CLAIM REJECTIONS – 35.U.S.C. §112,

Claim 1, and 2 – 6 stand rejected under 35 U.S.C. §112, second paragraph for reasons of record.

Applicants are amending the application to cancel claims 1-6 without prejudice.

Reconsideration and withdrawal of these grounds of rejection are urged.

Claims 1-46 stand rejected under 35 U.S.C.§112, second paragraph, for being indefinite in that the phrase "to lower viral RNA" in claims 1-6 or "to lower HCV-RNA" in claims 7-46 is indefinite.

Applicants are amending the application to cancel claims 1-6 and are amending claims 7-46 to replace "to lower HCV-RNA" with "to substantially lower HCV-RNA".

Basis for the amendment in claims 7-46 is found, for example, in the specification on page 6, lines 11-18.

Reconsideration and withdrawal of these grounds of rejection are urged.

Claims 1-6 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite in use of the phrase "susceptible viral infection".

Applicants assert that one skilled in the art reading the definition of susceptible viral infections on page 4, line 19 to page 5, line 11 would understand the metes and bounds of invention. However, to advance prosecution, Applicants are amending the application by canceling claims 1-6 without prejudice.

Claims 13, 15, 16, 26-29, 34, and 42-46 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite in the use of abbreviations: "3MIU", "PO", and "QW".

Applicants are amending the application to spell out these abbreviations in the claims where these abbreviations are first used, and to correct obvious typographical errors in claims 30 and 36. Basis for this amendment is found, for example, on page 15, line 1 to page 17, line 26.

Reconsideration and withdrawal of this ground of rejection are urged.

Claims 1-9, 13-21, 26-28, 42 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to enable treatment of all viral infections or the use of any and all antioxidants.

Applicants note that it is acknowledged that the specification is enabling for reducing hemolysis by administering Vitamin E during treatment of HCV with interferon and ribavirin.

Applicants are amending this application to cancel claims 1-6 without prejudice.

Applicants assert that the specification enables one skilled in the art to practice the pending claims 7-46 in light of the specification. See, for example, page 5, line 12 to page 6, line 5, where Applicants report use of a combination of Vitamin C and Vitamin E to ameliorate ribavirin hemolytic anemic during the administration of ribavirin and interferon alfa HCV combination therapy. Ribavirin hemolytic anemia during the administration of the aforesaid HCV combination therapy is evidenced by hemoglobin drops – See, for example, the specification on page 5, line 27 to page 6, line 5. Hemoglobin drops normally require ribavirin dose reduction. However, the use of antioxidants, for example, vitamins E and C in association with the HCV combination therapy in accordance with the claimed invention **markedly lowered the severity of the ribavirin-related hemolytic anemia**. It was noteworthy that no patients receiving the antioxidants in accordance with this invention needed to reduce the ribavirin dose. However, three of the control patients-who did not receive the antioxidants- required ribavirin dose reduction. (See page 5, line 33 to page 6, line 5).

Applicants list on page 6; line 20 to page 10, line 22, antioxidants and dosages and dose regimens sufficient to enable the skilled artisan to practice the invention of claims 13-21, 26-38, 42 and 43 in light of the specification.

Reconsideration and withdrawal of this ground of rejection are urged.

CLAIMS REJECTIONS – 35 USC§103(a)

Claims 1-16, 17-35 and 37-46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, Vol. 339, pages 1485-1492), Davis et al. (New England Journal of medicine, 1998, Vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, Vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, Vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, Vol. 42, pages 731-747).

McHutchinson et al., David et al., Poynard et al., and Reichard et al. each teach the use of interferon a-2b in combination with ribavirin to treat HCV. These four references fail to teach use of antioxidants to treat ribavirin-induced hemolysis. Only ribavirin dose reduction is taught.

None of the deficiencies of these four references are cured by Abella et al. which discloses the evaluation of the antioxidant activity of Vitamin E in the plasma of healthy volunteers to which an oxygen free radical initiator ("AAPH") was added. Nowhere in Abella et al. is there any teaching about treating HCV patients or ribavirin -induced anemia, much less any suggestion that Vitamin E, alone or in combination with Vitamin C would be useful in treating ribavirin –induced hemolysis in HCV patients being treated with the ribavirin-interferon alfa combination therapy. Applicants assert that there is no motivation in the references alone or in combination to make the modification needed to bridge the gap to the claimed invention.

Reconsideration and withdrawal of this ground of rejection are urged.

Claims 17 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499,), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol.,

1996, vol. 42, pages 731-747) as applied to claims 1-16, 17-35, and 37-46 above, and further in view of U.S. Patent 4917888 (Katre et al., 1990 and ", The '888 patent")

The '888 patent discloses various pegylated proteins but cures none of the deficiencies in McHutchison, et al., Davis, et al., Poynard, et al., Reichard, et al., or Abella et al., alone or in combination.

None of these six references, alone or in combination teach use of antioxdants in association with the ribavirin-interferon alfa HCV combinatino therapy to treat ribavirin-induced hemolysis.

Reconsideration and withdrawal of this ground of rejection are urged.

Applicants assert that the claimed invention, as amended, is in statutory compliance with 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. § 103(a).

Respectfully submitted,

Thomas D. Hoffman
Attorney of Record for Applicant
Reg. No. 28221
(908) 298-5037

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

December 17, 2001
Date of Deposit

THOMAS D. HOFFMAN
Registered Representative

Signature

12/17/2001
Date of Signature

APPENDIX

Claims marked up to show the amendments

7(amended). A method of treating a patient having chronic HCV infection which comprises administering to said patient a therapeutically effective amount of a combination therapy of interferon-alfa and ribavirin for a time sufficient to substantially lower HCV-RNA in association with a therapeutically effective amount of an antioxidant for a time sufficient to ameliorate ribavirin-related hemolysis.

9(amended). The method of claim 7 wherein the antioxidant is Vitamin A, Vitamin E, Vitamin C, coenzyme-Q10,[BHA] butylated hydroxylanisole ("BHA"),[BHT]butylated hydroxyltoluene ("BHT"), N-acetylcysteine, selenium, [panavir] 4,4'-isopropylidenedithiobis-2,6-di-t-butylphenol("panavir"), silybum marianum, lycopene, or mixtures thereof.

13(amended). The method of claim 7 wherein the combination therapy comprising 3[MIU, TIW] Million International Units ("MIU"), three times a week ("TIW") of interferon alfa-2b and about 600 mg to about 1600 mg/day [PO] orally ("PO") of ribavirin is administered for a first time period of at least about 24 weeks.

17(amended). The method of claim 7 wherein the combination therapy comprises about 0.5 to about 1.5 μg/kg[/day QW], once a week ("QW") of pegylated interferon alfa-2b and about 600 to about 1600 mg/day of ribavirin.

20(amended). A method of treating a patient having a chronic HCV infection which comprises administering to said patient for a first time period of at least about 24 weeks a therapeutically effective amount of interferon alfa and ribavirin sufficient to substantially lower detectable HCV-RNA in association with a therapeutically effective amount of an antioxidant sufficient to ameliorate ribavirin-related hemolysis.

30(amended). The method of claim 20 wherein the combination therapy comprises about 0.5 to about 1.5 μg/kg[/day], QW of pegylated interferon alfa-2b and about 600 to about 1600 mg/day of ribavirin.

32(amended). A method of treating a patient having a chronic HCV infection which comprises (a) administering to said patient for a first time period a therapeutically effective amount of a combination therapy of interferon alfa and ribavirin sufficient to substantially lower detectable HCV-RNA in association with a therapeutically effective amount of an antioxidant sufficient to ameliorate ribavirin-related hemolysis; and (b) thereafter administering about 600 to about 1600 mg/day of ribavirin in association with the antioxidant for a second time period of at least about 24 weeks after the end of the first time period.

36(amended). The method of claim 32 wherein the combination therapy comprises about 0.5 to about 1.5 μg/kg[/day], QW of pegylated interferon alfa-2b and about 600 to about 1600 mg/day of ribavirin.